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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,038	SLACK ET AL.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/30/2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-13 and 18-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-13 and 18-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/30/2009 has been entered.

Claim Status

Claims 1, 6-13, and 18-34 are pending. Claims 1, 18, 21 and 24 are amended. Claims 2-5 and 14-17 are cancelled. Claims 1, 6-13, and 18-34 are under current examination.

Priority

This application claims benefit as a 371 of PCT/CH03/00830 (filed 12/17/2003) which claims benefit of 60/434,790 (filed 12/18/2002). The instant application has been granted the benefit date, 18 December 2002, from the application 60/434,790.

RESPONSE TO ARGUMENTS

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6-13, and 18-34 remain rejected under 35 U.S.C. 103(a) as being obvious over Margolskee (US-5,817,759, issued 6 October 1998) in view of Yao et al.

(US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873) for the reasons of record and the comments below.

Applicant's arguments (Remarks, pages 7-21) and claim amendments have been fully considered but are not persuasive.

Therefore, the examiner hereby maintains the rejection of Claims 1, 6-13, and 18-34 under 35 U.S.C. 103(a) as being obvious over Margolskee (US-5,817,759, issued 6 October 1998) in view of Yao et al. (US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873).

The examiner expresses his appreciation for the thoughtful clarity and refreshingly straightforward analysis provided in the applicant's arguments.

The applicant's remarks raise several specific issues, but fundamentally form a general argument that the references cited in the obviousness rejection and subsequent post-filing art do not "show a high enough degree of predictability to render the applicants instant claims obvious" (Remarks, page 7, parag. 3). The examiner respectfully disagrees with the applicant's reasoning for the following reasons:

The applicant argues unpredictability because "changes in the constituents of the chimera may affect the three dimensional shape and other required functionalities, including, in particular, promiscuity…[and] signal strength" (Remarks, page 9, last paragraph). The examiner agrees, in principle, with the applicant's statement; however, the cited art teaches the criticality of the 44 amino-terminus of sensory G-proteins and particularly teaches the 44 amino terminus of Gustducin, SEQ ID NO:2. Therefore, the general application of the art recognized concept that "changes in the

constituents of the chimera may affect the three dimensional shape and other required functionalities" does not apply in the instant case, because of the important teachings of the art regarding the 44 amino-terminus of sensory G-proteins and particularly teaches the 44 amino terminus of Gustducin, SEQ ID NO:2. This structural portion is extremely important to the function; therefore the structure-function relationship is not unknown or highly variable.)). Therefore, the examiner finds the applicant's argument unpersuasive.

The applicant also argues unpredictability (Remarks, pages 9-11) because Yao fails to demonstrate promiscuity and only discloses a functional test for bitter receptor, so it is unclear whether the receptors will also work for sweet/umami. Currently, the instant claims do not require more than binding to one of the human bitter, sweet, and umami taste receptors (e.g., claim 24). The teachings of the cited art satisfy the limitations of the instant claims. The applicant seems to be arguing limitations which are not explicit in the claims (See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993) regarding arguing limitations which are not explicit in the claims). Therefore, the examiner finds the applicant's argument unpersuasive.

The applicant makes a similar argument (Remarks, page 14), indicating that signal strength of the chimeric G-protein suggested by the cited would be unpredictable. The applicant seems to be arguing limitations which are not explicit in the claims. Therefore, the examiner finds the applicant's argument unpersuasive.

The applicant uses a straw-man argument to argue (Remarks, pages 11-13) unpredictability by construing the teachings of post-filing art, Ueda et al. (*Journal of*

Neuroscience, Aug. 13, 2003; 23(19):7376-7380) as providing support for the unpredictability of the claimed invention as suggested by the cited art. Ueda et al. teach chimeric G-proteins having $G_{\alpha 15}$ or $G_{\alpha 16}$ wherein the C-terminus of the $G_{\alpha 15}$ or $G_{\alpha 16}$ are replaced by several alternative C-terminal amino acids of Gustducin, including the terminal 5, 11, 37 and 44 amino acids. Ueda et al. teach that only the 37 and 44 C-terminal amino acids provide functional chimeric G-proteins. This is consistent with the teachings of Margolskee who teaches "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical. The carboxyl terminal identity is of particular importance because it encompasses the site that has been implicated in G protein/receptor interactions" (col.9, lines 13-16, emphasis added by examiner). It would be surprising if the most highly conserved region of the C-terminus did not contain important functionality. Despite these teachings, the applicant suggests that because Ueda et al. teach the G16/gust23, G16/gust11, and G16/gust5 did not respond to known ligands, while G16/gust37 and G16/gust44 did, that there is unpredictability in suggesting a substitution of any of the C-terminal 5, 11, 23, 37 and 44 amino acids of Gustducin in chimeric G-proteins. The examiner believes this argument to be fallacious because the cited art suggests a preferred substitution of C-terminal amino acids 37 to 44 of Gustducin. Creating an argument (of unpredictability) against substituting any of the C-terminal amino acids 5, 11, or 23 of Gustducin in a chimeric G-protein does not bolster an argument against a preferred substitution of C-terminal amino acids 37 to 44 of Gustducin. Rather than supporting unpredictability, the

examiner believes Ueda et al. actually demonstrates the predictability of making the claimed invention, using the teachings of by Margolskee, Yao, and Ruiz-Avila et al. In the examiner's view, Ueda et al. has, in fact, demonstrated the predictability of success by showing that all the structural features present in C-terminal amino acids 37 to 44 of Gustducin are required for functional chimeric G-proteins. Therefore, the examiner finds the applicant's argument unpersuasive.

The applicant has also argued a secondary issue, regarding the issue of the degree of homology described in the art required to function successfully. Ordinarily, examiners in the examiner's work group (Art Units 1631-1639) would have rejected the instant claims under 35 USC 112, 1st paragraph (written description) because the claims are directed to chimeric G-proteins having 80% homology to the chimeric G-proteins of claim 1, wherein the chimeric protein binds to one or more of the human bitter, sweet and umami taste receptors (e.g., claim 24). However, when the examiner applied the Written Description Guidelines (March 25, 2008, Revision 1) he found that given the state of the art, particularly the knowledge of the state of the art regarding the C-terminal 44 amino acids of G-proteins, there was sufficient description of the degree of homology described in the art required for chimeric G-proteins of claim 1 to function successfully. Both Margolskee and Ruiz-Avila et al., indicate that the carboxy terminus is important to the function of sensation-specific G proteins. Margolskee teaches "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical. The carboxyl terminal identity is of particular importance because it

encompasses the site that has been implicated in G protein/receptor interactions" (col.9, lines 13-16, emphasis added by examiner). Yao et al. suggests "chimeric G_q variants and the isolated nucleic acids encoding the same. In one embodiment, the chimeric G_q protein variants comprise C-terminal sequences from transducin or $G\alpha_{olf}$." (col.3, lines 10-13) and Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace…up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ " (col.5, lines 16-19 and 22-23); the examiner believes there is ample suggestion of the claimed invention to the scope of 80% homology, because the structure and function are well characterized. Further regarding the homology argument, Margolskee teaches "among mammals…the α subunits of gustducin and the transducins comprise a subfamily of closely related proteins" (col.8, lines 66-67 and col.9, lines 1-2). Ruiz-Avila et al. seems to suggest both (1) the strong homology between gustducin and the transducins and (2) the importance of the C-terminus, "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. A key result of these studies is that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results). So regardless of the overall "low 58% homology" between gustducin and transducin, the portion important for function (44 amino acids of the carboxy terminus), there is a much greater homology. Because the critical structural features required for function were known in the art, the examiner concludes that a skilled artisan would know which C-terminal amino acids would be required to make such chimeric G-proteins comprising the 44

amino-terminus of Gustducin. Therefore, the examiner finds the art provides adequate description of the degree of homology required for the chimeric G-protein to function successfully.

Accordingly, the examiner finds the applicant's arguments unpersuasive and hereby maintains the instant rejection.

The examiner reiterates the pending rejection below:

Claims 1, 6-13, and 18-34 are rejected under 35 U.S.C. 103(a) as being obvious over Margolskee (US-5,817,759, issued 6 October 1998) in view of Yao et al. (US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873).

Claim 1 is directed to a G16/gust44 or G15/gust44 chimeric G-protein wherein the last 44 amino acids of the G16/gust44 or G15/gust44 protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of SEQ ID NO:2. While the claims lack clarity, the examiner is interpreting them as meaning that the applicant is claiming isolated chimeric G-proteins, G16/gust44 or G15/gust44. According to the specification chimeric G-proteins G16/gust44 or G15/gust44 comprise $G_{\alpha 15}$ or $G_{\alpha 16}$ wherein the 44 amino acid C-terminus of the $G_{\alpha 15}$ or $G_{\alpha 16}$ are replaced by the C-terminal 44 amino acids of Gustducin, described by SEQ ID NO:2.

Margolskee teaches "the α subunit of a novel taste receptor cell specific G protein, gustducin, or fragments and variants of the α subunit" (col. 3, lines 3-5). In addition, Margolskee teaches G-proteins which are $G_{\alpha 15\text{-Gustducin}}$ or $G_{\alpha\ 16\text{-Gustducin,}}$ of the

subtypes of G-proteins, $G_{\alpha 15}$ and $G_{\alpha 16}$ (col.2, line 4). Margolskee teaches, "Gustducin α subunit variants…may comprise polypeptide analogs wherein one or more of the specified amino acids is deleted or replaced or wherein one or more nonspecified amino acids are added" (col.3, lines 48-51). Margolskee also teach "among mammals, a 1 to 3% difference in amino acids identity is typical among α isotypes, suggesting that the α subunits of gustducin and the transducins comprise a subfamily of closely related proteins" (col.8, lines 66-67 and col.9, lines 1-2). Margolskee "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical. The carboxyl terminal identity is of particular importance because it encompasses the site that has been implicated in G protein/receptor interactions" (col.9, lines 13-16). In addition, Margolskee teach SEQ ID NO:3 which consists of the last 40 amino acids of Gustducin α subunit and is 100% identical to the last 40 of SEQ ID NO:2 of the instant application.

While Margolskee teach Gustducin α subunit variants and the importance of the carboxy 40 amino acids, Margolskee do not teach chimeric G-proteins comprising the carboxy 40 amino acids of Gustducin α subunit.

Yao et al. teach "chimeric G_q variants and the isolated nucleic acids encoding the same. In one embodiment, the chimeric G_q protein variants comprise C-terminal sequences from transducin or $G\alpha_{olf}$." (col.3, lines 10-13). Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace by at least about five amino acids from the C terminus of $G\alpha_{olf}$ or transducin" (col.5, line 16-19) and "up to 44 amino acids of the C terminus of transducin

or $G\alpha_{olf}$ may be incorporated" (col.5, lines 22-23). Yao et al. indicated that the C-terminus of Gα proteins can be modified to promote promiscuity of taste receptors. Yao et al. also describe the shared homologies of Gα subunits. Further, Yao et al. also suggest that the gustducin-coupled bitter receptor can be modified to increase promiscuity with regard to GPCR coupling (col.4, lines 35-55). In particular, Yao et al. show that their chimeric G-protein wherein the C terminus of the G_q-protein is replaced by 44 amino acids of transducin has functional activity with the Taste Receptor (col.8, Table I, and Examples).

Ruiz-Avila et al. teach "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. A key result of these studies is that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results).

Consequently, claim 1 would be obvious, in light of the teachings of Margolskee and Yao et al. and Ruiz-Avila et al.

Claims 6-9 are directed to nucleic acids encoding the claimed chimeric G-proteins, vectors comprising said nucleic acids, and cells comprising said vectors. The cited references are obvious over these limitations.

Claim 10 is directed to methods of producing a chimeric G-protein of claim 1 by recombinant technology. Margolskee teaches, "large scale production of gustducin α subunit polypeptides" by recombinant methods (col. 3, line 24-35). Margolskee teaches stably transformed host cells comprising the expression vector (col.3, line 24).

Claim 11 is directed to a method of analysis and discovery of modulators of bitter taste receptors using the chimeric proteins of claim 1. Margolskee teaches, "methods for identifying taste modifying agents having the capability to affect interactions between the gustducin α subunit and taste receptors or effectors and also describes methods for utilizing such taste modifying agents to modify taste by mimicking or inhibiting...bitter." (col. 4, lines 52-56).

Claims 12-13 are directed to a method of claim 11, wherein the assay is a mammalian cell-based assay. Margolskee teaches such mammalian cell-based assays that measure changes in intracellular messengers, including phosphodiesterase (col.13, lines 4-21) which affects Ca^{2+} and IP3 production.

Claim 18 is directed to a $G_{\alpha q\text{-}Gustducin}$ chimeric G-protein wherein the last 44 amino acids of the $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of SEQ ID NO: 2 and wherein the resulting $G_{\alpha q\text{-}Gust44}$ chimeric G-protein has a sequence homology of at least 80% in the last 44 amino acids of SEQ ID NO: 2.

Margolskee teaches "the α subunit of a novel taste receptor cell specific G protein, gustducin, or fragments and variants of the α subunit" (col. 3, lines 3-5). Margolskee teaches, "Gustducin α subunit variants…may comprise polypeptide analogs wherein one or more of the specified amino acids is deleted or replaced or wherein one or more nonspecified amino acids are added" (col.3, lines 48-51). Margolskee also teach "among mammals, a 1 to 3% difference in amino acids identity is typical among α isotypes, suggesting that the α subunits of gustducin and the transducins comprise a

subfamily of closely related proteins" (col.8, lines 66-67 and col.9, lines 1-2). Margolskee "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical. The carboxyl terminal identity is of particular importance because it encompasses the site that has been implicated in G protein/receptor interactions" (col.9, lines 13-16). In addition, Margolskee teach SEQ ID NO:3 which consists of the last 40 amino acids of Gustducin α subunit and is 100% identical to the last 40 amino acids of SEQ ID NO:2 of the instant application. Margolskee teaches, $G_{\alpha 15}$ and $G_{\alpha 16}$ (col.2, line 4). Margolskee teaches, "large scale production of gustducin α subunit polypeptides" by recombinant methods (col. 3, line 24-35). Margolskee teaches stably transformed host cells comprising the expression vector (col.3, line 24). Margolskee teaches, "methods for identifying taste modifying agents having the capability to affect interactions between the gustducin α subunit and taste receptors or effectors and also describes methods for utilizing such taste modifying agents to modify taste by mimicking or inhibiting...bitter." (col. 4, lines 52-56). Margolskee teaches such mammalian cell-based assays that measure changes in intracellular messengers, including phosphodiesterase (col.13, lines 4-21) which affects Ca^{2+} and IP3 production.

While Margolskee teach Gustducin α subunit variants and the importance of the carboxy 40 amino acids, Margolskee do not teach chimeric G-proteins comprising the carboxy 40 amino acids of Gustducin α subunit. Margolskee does not specifically teach the $G_{\alpha q\text{-Gustducin}}$ chimeric G-protein and also does not specifically recite replacement of the C-terminal sequence 44 amino acids of the gustducin receptor.

Yao et al. teach "chimeric G_q variants and the isolated nucleic acids encoding the same. In one embodiment, the chimeric G_q protein variants comprise C-terminal sequences from transducin or $G\alpha_{olf}$." (col.3, lines 10-13). Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace by at least about five amino acids from the C terminus of $G\alpha_{olf}$ or transducin" (col.5, line 16-19) and "up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ may be incorporated" (col.5, lines 22-23). Yao et al. indicated that the C-terminus of Gα proteins can be modified to promote promiscuity of taste receptors. Yao et al. also describe the shared homologies of Gα subunits. Further, Yao et al. also suggest that the gustducin-coupled bitter receptor can be modified to increase promiscuity with regard to GPCR coupling (col.4, lines 35-55). In particular, Yao et al. show that their chimeric G-protein wherein the C terminus of the G_q-protein is replaced by 44 amino acids of transducin has functional activity with the Taste Receptor (col.8, Table I, and Examples).

Yao et al. teach, $G_{\alpha q}$ chimeric G-proteins (col.4, lines 12-27). In particular, the chimeric proteins described, combine various $G\alpha_q$ class proteins. Yao et al. also teach chimeric G-proteins that comprise C-terminal sequences from Transducin and $G\alpha_{olf}$ (col3, lines 12-13).

Yao et al. also teach analysis and discovery of agonists and antagonists of chemosensory receptors, using G_q-protein variants (col.3, lines 15-30), including the "gustducin-coupled bitter receptor" (col.4, line 53). Yao et al. further suggest that modulators could be used in "protein pharmaceutical and food industries" (col.4, line

32). Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace by at least about five amino acids from the C terminus of $G\alpha_{olf}$ or transducin" (col.5, line 16-19) and "up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ may be incorporated" (col.5, lines 22-23). Consequently, claims 3-4 would be obvious, in light of the teachings of Yao et al.

While Yao et al. also teach chimeric G-proteins that comprise C-terminal sequences from Transducin and $G\alpha_{olf}$ (col3, lines 12-13) and Yao et al. indicated that the C-terminus of Gα proteins can be modified to promote promiscuity of taste receptors, Yao et al. does not specifically teach a $G\alpha_{q\text{-}Gustducin}$ chimeric G-protein having a C-terminal 44 amino acid substitution from Gustducin.

Ruiz-Avila et al. teach the nexus of gustducin and transducin homology and the importance of the C-terminus for interacting with taste receptors. Ruiz-Avila et al. teach "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. A key result of these studies is that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results).

Consequently, all of the instant claims would be obvious, in light of the teachings of Margolskee and Yao et al. and Ruiz-Avila et al.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to make a $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of Gustducin.

The person of ordinary skill in the art would have been motivated to make this protein because, "C-terminal substitution increases promiscuity of said variant G, protein as compared to the corresponding native G_q protein" (Yao et al. col.5, lines 20-22). While Yao et al. does not specifically teach making a chimera between G_q protein and gustducin, it is clearly obvious in light of the teachings involving substitutions with C-terminal sequences from other chemosensory molecules, transducin and $G\alpha_{olf}$). In particular, Yao et al. show that their chimeric G-protein wherein the C terminus of the G_q-protein is replaced by 44 amino acids of transducin has functional activity with the Taste Receptor (col.8, Table I, and Examples). Additionally, Margolskee teach that the carboxy terminal 40 amino acids of Gustducin are important for G protein/receptor interactions. Furthermore, Margolskee teach "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical." Ruiz-Avila et al. teach "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. A key result of these studies is that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results). Furthermore, Yao et al. suggest that analysis and discovery of agonists and antagonists of chemosensory receptors, using G_q-protein variants can be performed using chimeric proteins and actually mention gustducin bitter receptor as a receptor which might be useful "to customize sensory perception" (col.4, line 32-33).

In addition, to the strong suggestion to make a $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of Gustducin by the combined teachings of Margolskee in view of Yao et al. and further in view of Ruiz-Avila et al., there is another rationale for combining prior art elements according to known methods to yield predictable results. All of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (chimeric $G\alpha_q$-proteins and methods of using them; a suggestion of the importance of the c-terminal 44 amino acids of Gustducin and related G-proteins; knowledge that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors; and the knowledge that the C-terminus of Gα proteins can be modified to promote promiscuity of taste receptors) are taught by Margolskee or Yao or Ruiz-Avila et al. It would be therefore predictably obvious to use a combination of these elements in a vaccine. The methods of using these chimeric G-proteins are further known in the art and are predictable; therefore they are likewise obvious.

An artisan would have expected success, because Yao et al. were successful in making similar chimeric G-proteins with other chemosensory receptors. Absent evidence to the contrary, there is no reason to believe that making a $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of Gustducin would not be successful.

Therefore the products and methods as taught by Margolskee in view of Yao et al. and further in view of Ruiz-Avila et al. would have been *prima facie* obvious over the method of the instant application.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6-13, and 18-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 has been amended to recite a G16/gust44 or G15/gust44 chimeric G-protein wherein the last 44 amino acids of the G16/gust44 or G15/gust44 protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of SEQ ID NO:2. The examiner has deduced that chimeric G-proteins G16/gust44 or G15/gust44 comprise $G_{\alpha 15}$ or $G_{\alpha 16}$ wherein the 44 amino acid C-terminus of the $G_{\alpha 15}$ or $G_{\alpha 16}$ are replaced by the C-terminal 44 amino acids of Gustducin, described by SEQ ID NO:2. The newly amended claims seem to be replacing the 44 amino acid C-terminus of the G16/gust44 or G15/gust44 G-proteins with the C-terminal 44 amino acids of Gustducin, described by SEQ ID NO:2.

However, the terms "G16/gust44" and "G15/gust44" are not specifically defined in the specification. In fact, "G15/gust44" is not mentioned in the specification or originally filed claims. G16/gust44 is non-scientific shorthand nomenclature which is scarcely mentioned in the instant specification. It is impossible for a skilled artisan to know exactly what is encompassed by the terms "G16/gust44" and "G15/gust44." The new claim amendments have decreased the clarity of the claims. Therefore, the metes and bounds of the instant claims is unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-13, and 18-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Claim 1 has been amended to recite a G16/gust44 or G15/gust44 chimeric G-protein wherein the last 44 amino acids of the G16/gust44 or G15/gust44 protein

sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of SEQ ID NO:2.

The term "G15/gust44" is not mentioned in the specification or originally filed claims. Therefore, this term is new matter.

Furthermore, the amended claims seem to be describing a chimeric G-protein which has not been previously described in the instant claims. The newly amended claims seem to be replacing the 44 amino acid C-terminus of the G16/gust44 or G15/gust44 G-proteins with the C-terminal 44 amino acids of Gustducin, described by SEQ ID NO:2. The previous claims described a chimeric G-protein which comprises $G_{\alpha 15}$ or $G_{\alpha 16}$ and wherein the 44 amino acid C-terminus of the $G_{\alpha 15}$ or $G_{\alpha 16}$ are replaced by the C-terminal 44 amino acids of Gustducin, described by SEQ ID NO:2. Based upon the vagueness of the terms "G16/gust44" and "G15/gust44," it seems the previous and currently pending claims are directed to different structures. Therefore, claims directed to chimeric G-proteins "G16/gust44" and "G15/gust44," having substituted amino termini seems to be new matter.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Scott Long/
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